Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Review

Honey in modern wound care: A systematic review

L. Vandamme [1,*], A. Heyneman [1], H. Hoeksema, J. Verbelen, S. Monstrey

Department of Plastic & Reconstructive Surgery – Burn Centre, Ghent University Hospital, Ghent, Belgium

ARTICLE INFO

Article history:
Accepted 19 June 2013

Keywords:
Honey
Wound healing
Design
Methodology

ABSTRACT

Honey, known for centuries as a topical treatment for a wide range of wounds, has recently known a revival in modern wound care. The objective of this systematic review is to evaluate the available evidence and the role of honey in contemporary wound care. The search strategy was developed in the databases PubMed and ISI Web of Science. Fifty-five studies of any design, evaluating the use of honey in human burns, ulcers and other wounds, written in English, French, German or Dutch were eligible for inclusion. In all three wound categories honey seems to be a dressing with wound healing stimulating properties. In burns there is also evidence for its antibacterial capacity. In general, honey is also been mentioned to have deodorizing, debridement, anti-inflammatory and wound pain reducing properties, although the evidence for these properties is rather limited. Many of the included studies have methodological problems, and the quality of certain studies is low, making it difficult to formulate conclusive guidelines. This review reveals several gaps in the research of honey in modern wound care, and recommendations are suggested for future research.

Contents

1. Introduction . . . 1515
2. Methods . . . 1515
3. Results . . . 1516
   3.1. Description of the included studies . . . 1516
4. Outcomes . . . 1516
   4.1. Burns . . . 1516
   4.2. Ulcers . . . 1517
   4.3. Other wounds . . . 1521
5. Discussion . . . 1521
   5.1. Outcomes of the included studies . . . 1521
   5.2. Methodology of the included studies . . . 1522
   5.3. Strengths and weaknesses of this review . . . 1522
   5.4. Recommendations for future research . . . 1522
   References . . . 1523

* *Corresponding author at*: Department of Plastic & Reconstructive Surgery – Burn Centre, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium. Tel.: +32 0 477 68 93 32; fax: +32 0 54 33 26 76.
E-mail address: lynn.vandamme@ugent.be (L. Vandamme).

[1] Both authors are shared first authors of this publication.

0305-4179/$36.00
http://dx.doi.org/10.1016/j.burns.2013.06.014

1. Introduction

Since ancient times, as discovered in the tomb of King Tut (14th century BC), honey has occupied an important place in traditional medicine and has been mentioned as a medicinal product in countless works [1–5]. Probably the first deliberate mentioning of honey as a wound treatment was found in the ''Edwin Smith papyrus'' (2600–2200 BC) [6]. Not only the Egyptians but also the ancient Greeks and Romans used honey, not only in combination with vegetable or animal fat but also as part of all sorts of ointments, which were used to prevent wounds from festering [4,6–8]. Avicenna (980–1037), the most famous of the Arab doctors of Islam, advised the use of astringents such as cooked honey and myrrh to reduce the amount of exudate in wounds with tissue loss [9]. From the early Middle Ages to the late 19th century, there were several descriptions of the use of honey to cleanse and heal chronic and traumatic wounds, in particular gunshot wounds in the 17th and 18th century [9,10]. In more recent times, during World War I, honey was used by the Russians and the Germans [4,11] and remained popular until the advent of antibiotics in 1940 [1,12]. However, due to the ever-increasing resistance against antibiotics and the growing awareness for natural remedies, the interest in the antimicrobial and wound healing properties of honey have shown a revival [1,3,13].

Honey is a viscous, hypersaturated sugar solution coming from nectar which has been collected and modified by the honey bee, Apis [6]. The bees collects the nectar of the plants, transform and combine it with substances of their own. The honey is stored in the honey comb to ripen and mature [14]. Honey primarily contains sugar (75–79%) and water (20%) [7]. Other components of honey are proteins, vitamins of the B complex, minerals and antioxidants such as flavonoids, ascorbic acid, catalase and selenium [11,15]. Organic acids make up 0.57% of the honey and are responsible for its acidity [15,16]. The main enzymes in honey are invertase, amylase and glucose oxidase [16]. The specific percentages of all these different components may vary depending on the plant origin, the geographical location, the season in which the honey was collected, the treatment of honey since its harvesting, and its age [8].

Honey is easily contaminated during its production process [16,17]. Therefore, a medical grade honey should be sterilized, not by heating, but by means of gamma irradiation [8]. Through the process of gamma irradiation, micro-organisms are killed without jeopardizing the antibacterial activity of the medical honey [8,18,19].

The antibacterial effect of honey is based on several mechanisms. First, hydrogen peroxide is produced by the enzyme glucose oxidase when the honey is diluted by wound exudate [1,11,16,17]. Hydrogen peroxide activates the neutrophils through the nuclear transcription factor NF-kB. Hereby genes are activated that produce cytokines which strengthen the inflammatory response by recruiting and activating leucocytes [14,20–22].

Phytochemicals, also called flavonoids, are a second antibacterial mechanism of honey [11,16], and are present in Manuka honey and Medihoney [8,23,24]. By their direct inhibition of phagocytosis, these antioxidants prevent the formation of the superoxide free radicals, protecting the tissues from further damage [14].

A third effect of honey relates to the fact that bacterial growth requires a water activity (amount of 'free' water) of 0.94–0.99. However, since honey has a low water activity of 0.56–0.62, this prevents the growth of bacteria [11,18]. The high sugar content of honey draws fluid from the wound by osmosis and hereby extracts water from the bacteria resulting in bacterial death [8,23].

Finally, the acidity of honey (with a pH between 3.2 and 4.5) further inhibits the growth of micro-organisms, since the optimal pH for the majority of these organisms lies between 7.2 and 7.4 [3,23,25].

Apart from its antibacterial effect, a lot of other properties have been attributed to honey. It has also been shown to reduce inflammation, to avoid the need for surgical debridement, to neutralize bad smells, and to accelerate tissue growth and wound healing [3].

In clinical practice, mainly Manuka honey and Medihoney are being used. Manuka honey is a mono-floral honey that comes from the Leptospermum scoparium tree in New Zealand and Australia and is particularly interesting because its antibacterial activity is independent of the peroxide activity [26–29]. Medihoney is a standard mix of Australian and New Zealand honeys, predominantly of the Leptospermum species (Manuka) [4,30,31]. It has an antibacterial activity that corresponds to a phenol acid strength of at least 18, which makes it currently the strongest antibacterial medical honey available [4]. Besides mono-floral honey, also multi-floral honey is used in clinical practice.

Honey, an ancient therapy, has known a revival in recent times and is frequently used nowadays for a very wide range of conditions. Despite its universal use, especially in the treatment of burn wounds and difficult to heal chronic ulcers, it is not clear to date what exactly the level of evidence is for honey in wound management [1,3,11,18,23,32]. The aim of this systematic review is to evaluate the use of honey in modern wound care based on the published literature to date. It examines the role of honey in wound care, the wound categories in which honey is applied, and provides a critical evaluation of the reported benefits of using honey.

2. Methods

This study was designed as a systematic review of published randomized controlled trials (RCTs), clinical controlled trials (CCTs), clinical trials (CTs) and case reports (CRs).

The search strategy was developed in two electronic databases: PubMed and ISI Web of Science by the first and the second author. Both databases were selected in order to cover most of the published peer-reviewed literature.

A search filter composed of four items: ''Honey'', ''Wound healing'', ''Design'' and ''Language'' was executed. These topics were combined using the Boolean operators ''AND'' and ''OR''. As ''Design'' the following research designs were included in the search: RCTs, CCTs, CTs, comparative studies and CRs; leading to five separate search filters. The languages included were English, French, German and Dutch. Both the

Table 1 – Search strategy for each database by topic.

PubMed	ISI Web of Science
(“honey”[MeSH Terms] OR “honey”[All Fields]) AND (“wound healing”[MeSH Terms] OR (“wound”[All Fields] AND “healing”[All Fields]) OR “wound healing”[All Fields]) AND (“randomized controlled trial”[Publication Type] OR “randomized controlled trials as topic”[MeSH Terms] OR “randomized controlled trial”[All Fields] OR “randomized controlled trial”[All Fields] OR “controlled clinical trial”[Publication Type] OR “controlled clinical trials as topic”[MeSH Terms] OR “controlled clinical trial”[All Fields] OR “clinical trial”[Publication Type] OR “clinical trials as topic”[MeSH Terms] OR “clinical trial”[All Fields] OR “comparative study”[Publication Type] OR “comparative study”[All Fields] OR “case reports”[Publication Type] OR “case reports”[All Fields]) AND (English[lang] OR French[lang] OR German[lang] OR Dutch[lang])	#1 AND #2 AND (#3 OR #5 OR #7 OR #9 OR #11) *Databases = SCI-EXPANDED, SSCI Timespan = All Years* *Lemmatization = On* #1 TS= honey #2 TS= wound healing #3 TS= randomized controlled trial #5 TS= controlled clinical trial #7 TS= clinical trial #9 TS= comparative study #11 TS= case report

TS: topics; lang: language.

American and British English spellings were included to avoid a possible loss of results. The five filters were then joined to form one major search filter (Table 1).

The last search in both databases took place on July 15, 2012. No search restrictions were applied with regard to year of publication, authors or participating institutions. Only the studies about the treatment of human burns, ulcers and other wounds (e.g. trauma, post-operative wounds,...) were eligible for inclusion in the review. The flow of publications was executed by the first two authors separately and their results were compared. In case of differing opinions, a third opinion was solicited.

The study parameters presented in Tables 4 and 5 were systematically included in the detailed analysis and methodological strengths or weaknesses were identified. Outcome parameters were grouped in six different categories (Table 2). All these items were listed and the findings were discussed between the authors.

3. Results

3.1. *Description of the included studies*

The search strategies in PubMed (PM) and Web of Science (WOS) resulted in a total of 55 unique publications (Fig. 1).

In three of the included publications a clarification regarding the selection of design is indicated.

Table 2 – Categories of outcome parameters.

Outcome group	Outcome parameter
Antibacterial effect	Reduction or eradication of bacteria
Healing stimulating properties	Reduction in wound size, healing time, complete healing, stimulation of granulation tissue and epithelialisation
Debriding effect	Reduction in slough, necrosis and debris
Anti-inflammatory effect	Reduction in redness, oedema, exudates and histopathologic inflammation.
Odour reducing capacity	Reduction in bad smell
Wound pain	Reduction in pain that was already present before honey was applied

The publication of Moolenaar et al. is actually a letter to the editor, but in this review it was selected as an RCT because it describes a fully randomized controlled study performed by the authors. The reporting was limited, but of sufficient value to include [33].

The publication of Dany-Mazeau and Pautard is a CCT under construction and had at the time of its publication only one third of the necessary number of patients recruited [7]. This interim publication discussed three cases. Therefore it was considered a case report in this review. The two articles are both the same, except for the language – one is written in French and the other in German. For that reason they were considered to be one publication.

Another remark is that the two publications from Gethin and Cowman [34,35] refer to the same study. In the first publication the primary outcomes are discussed, and in the other one the secondary outcomes. In this review, they are therefore included as two separate studies.

The 55 included publications enrolled various wound etiologies as burns, ulcers, and other types of wounds, such as mixed wounds, traumatic wounds and postoperative wounds (Table 3). Due to the heterogeneity of the studies, a meta-analysis could not be carried out.

4. Outcomes

The results of the included studies were examined and classified by wound aetiology.

4.1. *Burns*

Seven RCTs examined the effect of pure, unprocessed and undiluted honey in the treatment of burns (Table 4). In all seven, the *antibacterial effect* of honey had been investigated. Six reported a positive outcome for honey and in four of them there was a statistically significant difference in favour of honey (Tables 4 and 5). Only tangential excision (TE) with subsequent skin grafting leads to a better antibacterial result [36].

Six randomized trials investigated the *effects* of honey *on wound healing* and all six found statistically significant results in favour of honey for the time to complete healing

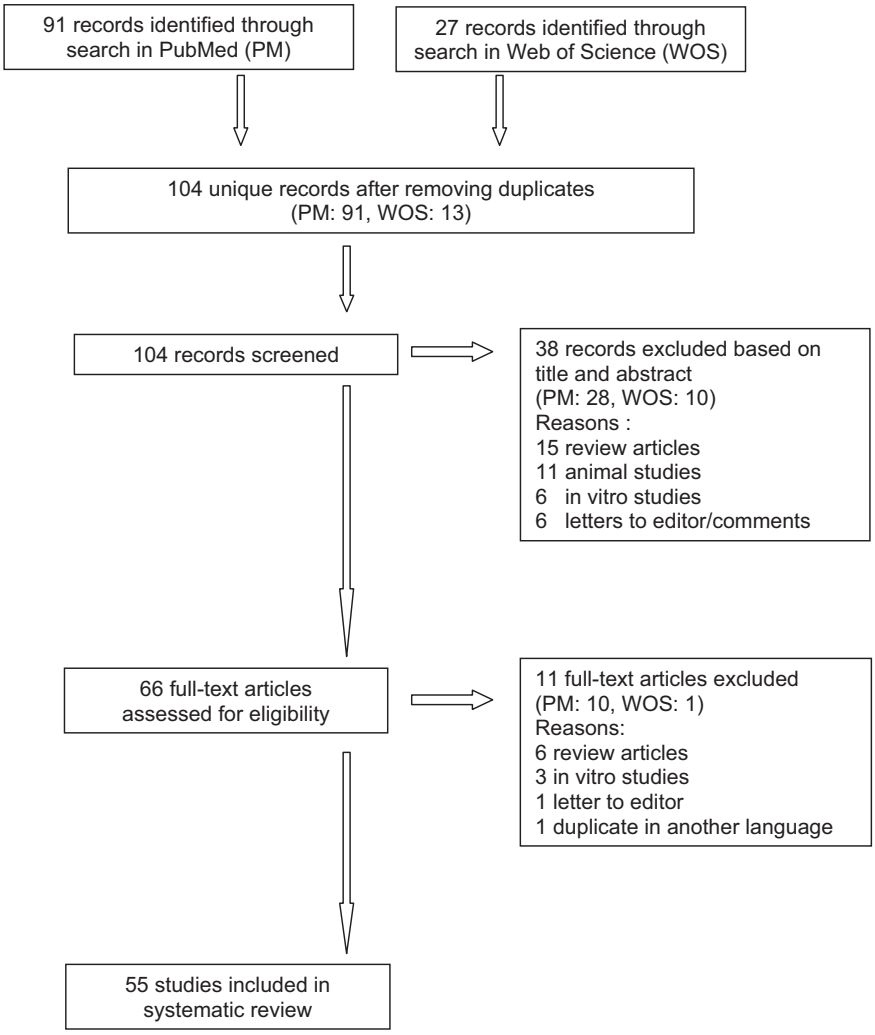

Fig. 1 – Flowchart of included studies.

(Tables 4 and 5). Three out of six also reported a faster epithelialization process with honey [37–39] and only two trials found a stimulating effect on the formation of healthy granulation tissue [40,41].

In four RCTs honey was compared to silver sulphadiazine (SSD). Remarkably, in two out of four trials honey even had a statistically significant better antibacterial effect in comparison to SSD; and in all four trials honey established a statistically significant faster wound healing in comparison to SSD, which still is considered the worldwide standard to date (Tables 4 and 5).

Table 3 – Overview wound etiologies by design.

Wound etiology	RCT	CCT	CT	CR	Total
Burns	7	0	0	0	7
Ulcers	5	1	4	9	19
Other	13	1	1	14	29
Total	25	2	5	23	55

The *debriding effect* of honey on burn wounds, as well as its *anti-inflammatory and odour reducing capacities* had been reported in a number of trials (Table 5). Some of these studies reported a positive effect of honey on these outcomes. However, if actually compared to the control group, they all showed non statistically significant results (Tables 4 and 5).

Three RCTs mention the *effect* of honey *on wound pain* (pain that was already present before honey was applied), and only one trial report a positive wound pain reducing effect in favour of honey (Tables 4 and 5).

It can be concluded that the evidence for the antibacterial and healing stimulating properties of honey is well substantiated. However, the available evidence for its debridement and anti-inflammatory effects as well as for its odour and wound pain reducing capacities is rather weak and as a result no real evidence based conclusions could be drawn.

4.2. *Ulcers*

Honey is widely used in various types of ulcers, such as venous, arterial and mixed ulcers, pressure ulcers and diabetic

Table 4 – Information of the included studies by wound category and design.

	Sample size	Type of therapy used	Wound aetiology
Burns: RCTs			
Baghel et al. [66]	*n* = 78: *H* = 37; *C* = 41	*H*: undiluted, pure; *C*: SSD	1st and 2nd degree burns TBSA < 50%
Malik et al. [39]	*n* = 150 (idd): *H* = 150; *C* = 150	*H*: Langnese; *C*: SSD	2nd degree burns TBSA < 40%
Subrahmanyam [40]	*n* = 104: *H* = 52; *C* = 52	*H*: pure, unprocessed, undiluted; *C*: SSD	Superficial thermal burns TBSA < 40%
Subrahmanyam [37]	*n* = 92: *H* = 46; *C* = 46	*H*: unprocessed, undiluted; *C*: polyurethane film (OpSite®)	Partial thickness burns TBSA < 40%
Subrahmanyam [41]	*n* = 100: *H* = 50; *C* = 50	*H*: pure, unprocessed, undiluted (Indian hive bee); *C*: boiled potato peel	Partial thickness burns TBSA < 40%
Subrahmanyam [38]	*n* = 50: *H* = 25; *C* = 25	*H*: pure, unprocessed, undiluted; *C*: SSD	Superficial theramal burns TBSA < 40%
Subrahmanyam [36]	*n* = 50: *H* = 25; *C* = 25	*H*: unprocessed (Indian hive bee); *C*: early TE and skin grafting	Burns TBSA <30% and full thickness
Ulcers: RCTs			
Gethin and Cowman [34]	*n* = 108: *H* = 54; *C* = 54	*H*: Manuka (Comvita), UMF 18+; *C*: hydrogel (IntraSite gel)	Venous leg ulcers
Gethin and Cowman [35]	*n* = 108: *H* = 54; *C* = 54	*H*: Manuka (Comvita), UMF 18+; *C*: hydrogel (IntraSite gel)	Venous leg ulcers
Jull et al. [27]	*n* = 368: *H* = 187; *C* = 181	*H*: Manuka (ApiNate™, Comvita), UMF 12+; *C*: standard dressings (alginate, foam, hydrofibre, hydrocolloid, hydrogel, non; adherent, iodine or silver)	Venous and mixed ulcers
Shukrimi et al. [67]	*n* = 30	*H*: clean, non-sterile, pure; *C*: povidone-iodine 10%	Wagner type II diabetic foot ulcers
Yapucu Güneş [65]	*n* = 50 wounds: *H* = 15; *C* = 11 (in 26 patients)	*H*: sterile, unprocessed (raw, natural, organic, unpasteurized) from one source, MIC = 3.8%; *C*: ethoxy-diaminoacridine plus nitrofurazone dressings	Stage II and III pressure ulcers
Ulcers: CCT			
Oluwatosin et al. [62]	*n* = 50 wounds (in 38 patients)	*H*: unprocessed and undiluted; *C*: phenytoin/honey mixture and phenytoin	Posttraumatic or post infective ulcers
Ulcers: CTs			
Biglari et al. [43]	*n* = 20	*H*: Medihoney (Comvita, New Zealand); C:/	Stage III and IV pressure ulcers
Gethin et al. [79]	*n* = 20 wounds (in 17 patients)	*H*: Manuka (Apinate®, Comvita); *C*: –	Venous, arterial, mixed and pressure ulcers
Moghazy et al. [47]	*n* = 30	*H*: pure, raw, untreated commercial (Alexandria University); *C*: no control group (patients themselves were considered control before starting honey dressing)	Diabetic foot ulcers
Schumacher [63]	*n* = 6	*H*: medical; *C*: –	Venous leg ulcers
Ulcers: CRs			
Alcaraz and Kelly [19]	*n* = 1	*H*: Medihoney; *C*: Aquacel® (ConvaTec)	Venous leg ulcer
Dunford [5]	*n* = 1	*H*: Medihoney; *C*: –	Venous leg ulcer
Eddy and Gideonsen [50]	*n* = 1	*H*: supermarket; *C*: –	Diabetic foot ulcers
Hampton et al. [46]	*n* = 1	*H*: Manuka (Algivon®); *C*: –	Mixed ulcers
Hendrickson [48]	*n* = 1	*H*: Medihoney® (Honeycolloid™); *C*: /	Cutaneous small-vessel vasculitis
Natarajan et al. [45]	*n* = 1	*H*: Manuka; *C*: –	Hydroxyurea-induced leg ulcer
Sare [4]	*n* = 3	*H*: Medihoney™; *C*: –	Venous and mixed leg ulcers
Van der Weyden [49]	*n* = 2	*H*: Manuka (Apinate), UMF 12+; *C*: –	Pressure ulcers
Van der Weyden [44]	*n* = 1	*H*: Manuka (Apinate), UMF 12+; *C*: –	Venous leg ulcer
Other: RCTs			
Abdulrhman et al. [74]	*n* = 90: *H* = 30; *C* = 30; HOPE = 30	*H*: non; sterile (Egypt); *C*: HOPE (mixture of honey, olive oil; propolis extract and beeswax) and benzocaine gel	Chemotherapy induced oral mucositis grades 2 and 3
Al-Waili and Saloom [70]	*n* = 50: *H* = 26; *C* = 24	*H*: crude, undiluted Yemini; *C*: spirit (70% ethanol) and povidone-iodine	Postoperative wound infections following caesarean sections and hysterectomies

Table 4 (*Continued*)

	Sample size	Type of therapy used	Wound aetiology
Chang et al. [77]	*n* = 48: *H* = 16; Budesonide = 16; Gentamicin = 16	*H*: Manuka (Montreal); *C*: normal saline solution	Chronic rhinosinusitis undergoing FESS (functional endoscopic sinus surgery)
English et al. [28]	*n* = 30: *H* = 14; *C* = 16	*H*: Manuka, UMF 15; *C*: Wrigley's 'Extra'™ sugarless chewing gum	Gingivitis
Ingle et al. [68]	*n* = 82: *H* = 42; *C* = 40	*H*: natural monofloral aloe; *C*: hydrogel (IntraSite Gel)	Traumatic skin lesions
Khanal et al. [69]	*n* = 40: *H* = 20; *C* = 20	*H*: honey from beehives Western Ghats forests, India; *C*: lignocaine gel	Radiation-induced oral mucositis
Lund-Nielsen et al. [75]	Initial 75, but 6 excluded, study based on *n* = 69: *H* = 34; *C* = 35	*H*: Manuka (Algivon, Activon), UMF 12+; *C*: nanocrystalline silver-coated bandage (Acticoat)	Malignant wounds
McIntosh and Thomson [76]	*n* = 100: *H* = 52; *C* = 48	*H*: Manuka (Apinate®); *C*: paraffin-impregnated tulle gras (Jelonet®)	Surgical toenail wounds
Moolenaar et al. [33]	*n* = 24: *H* = 12; *C* = 12	*H*: HoneySoft® (= Chilian medicinal multifloral); *C*: paraffin gauze (Unitulle®)	Radiotherapy-induced skin toxicity
Mphande et al. [72]	*n* = 40: *H* = 22; *C* = 18	*H*: honey from Malawi; *C*: sugar from Malawi	Mixed: chronic osteomyelitis, postsurgical wounds, ulcers and trauma.
Okeniyi et al. [71]	*n* = 43 wounds: *H* = 23; *C* = 20 (in 32 patients)	*H*: crude, undiluted; *C*: Edinburgh University solution of lime (EUSOL)	Abscess wounds
Robson et al. [15]	*n* = 105: *H* = 52; *C* = 53	*H*: Medihoney™; *C*: standard conventional treatment	Mixed: leg ulcers, breast wounds, eczema, and multiple other wounds
Robson et al. [73]	*n* = 49: *H* = 25; *C* = 24	*H*: Medihoney™, Antibacterial Wound Gel™; *C*: conventional dressings	Microvascular free tissue reconstruction for cancer of head and neck
Other: CCT			
Misirlioglu et al. [64]	*n* = 88 or 87 => Error in the study	*H*: unprocessed; *C*: paraffin gauzes and hydrocolloid dressings	Skin graft donor sites
Other: CT			
Efem [52]	*n* = 59	*H*: fresh, unprocessed; *C*: –	Mixed: gangreen, burns, and all sorts of ulcers (venous, pressure, traumatic, malignant,...)
Other: CRs			
Ahmed et al. [29]	*n* = 60	*H*: HoneySoft® (=Chilian medicinal multifloral); *C*: –	Mixed: surgical wounds, venous and pressure ulcers, vasculitis, scleroderma, traumatic skin lacerations, and burns
Alese and Irabor [80]	*n* = 1	*H*: /; *C*: –	Pyoderma gangrenosum
Chernev et al. [57]	*n* = 4	*H*: Medihoney (New Jersey); *C*: /	Mixed (infected leg wound, surgical wound, pressure ulcers)
Cooper et al. [53]	*n* = 1	*H*: Manuka; *C*: –	Surgical wound
Dany-Mazeau and Pautard [7]	*n* = 3	*H*: /; *C*: no control in two cases, Débrisan in the third case	Pressure ulcers, postoperative wounds and surgical wounds
Dunford [13]	*n* = 1	*H*: Medihoney from Australia; *C*: –	Wound infection and abdominal cellulitis following lymph node biopsy in a patient undergoing chemotherapy
Dunford et al. [26]	*n* = 2	*H*: Manuka, UMF 13; *C*: –	Traumatic skin lesions
Ganacias [58]	*n* = 1	*H*: Medihoney®; *C*: /	Postsurgical wound
Hon [81]	*n* = 1	*H*: Manuka (Activon Tulle); *C*: –	Epidermolysis bullosa
Lotfy et al. [54]	*n* = 1	*H*: /; *C*: –	Foot abscess in a diabetic patient
Robson and Cooper [56]	*n* = 4	*H*: Medihoney™; *C*: /	Wounds impaired by radiotherapy

Table 4 (*Continued*)

	Sample size	Type of therapy used	Wound aetiology
Rudzka-Nowak et al. [55]	*n* = 1	*H*: Manuka (Algivon, Activon); *C*: /	Phlegmonous and necrotic lesions in the abdominal integuments and lumbar region after traumatic colon rupture
Stephen-Haynes [25]	*n* = 20 (only 2 were extensively reported)	*H*: Manuka (Activon Tulle); *C*: –	Mixed: a variety of ulcers and sloughy, malodorous, non-healing wounds
Trudgian and Trotman [51]	*n* = 1	*H*: Manuka; *C*: /	Leg wound in Ehlers–Danlos syndrome

n: total sample size; *H*: honey group; *C*: control group; idd: intra-individual design; SSD: silver sulphadiazine; TBSA: total body surface area; TE: tangential excision; UMF: unique manuka factor; MIC: minimal inhibitory capacity; –: none; +: yes; /: not reported.

Table 5 – Outcomes of the included studies by wound category and design.

Outcome	Antibacterial effect	Healing	Debridement	Anti-inflammatory	Odour reduction	Wound pain reduction
Burns: RCTs						
Baghel et al. [66]	++	++	+	0	0	0
Malik et al. [39]	+	++	0	/	0	0
Subrahmanyam [40]	++	++	/	0	/	+
Subrahmanyam [37]	++	++	/	0	/	/
Subrahmanyam [41]	++	++	0	0	0	±
Subrahmanyam [38]	/	++	+	+	0	0
Subrahmanyam [36]	––	0	0	0	0	0
Ulcers: RCTs						
Gethin and Cowman [35]	+	0	0	0	0	++
Gethin and Cowman [34]	/	++	+	0	0	0
Jull et al. [27]	±	±	0	0	0	0
Shukrimi et al. [67]	±	±	0	+	+	0
Yapucu Güneş [65]	0	++	0	0	0	0
Ulcers: *CCT*						
Oluwatosin et al. [62]	0	–	0	0	0	±
Other wounds: RCTs						
Abdulrhman et al. [74]	0	++	0	0	0	0
Al-Waili and Saloom [70]	++	++	0	/	0	/
Chang et al. [77]	0	±	0	±	0	0
English et al. [28]	/	0	0	++	0	0
Ingle et al. [68]	0	+ (shallow wounds) and – (abrasions)	0	0	0	0
Khanal et al. [69]	0	++	0	++	0	0
Lund-Nielsen et al. [75]	0	±	±	±	±	±
McIntosh and Thomson [76]	0	–– (partial avulsion) and + (total avulsion)	0	0	0	±
Moolenaar et al. [33]	0	+	0	0	0	+
Mphande et al. [72]	+	+	0	0	0	+
Okeniyi et al. [71]	0	++	++	++	0	0
Robson et al. [15]	0	+	/	0	0	0
Robson et al. [73]	±	/	0	0	/	0
Other wounds: CCT						
Misirlioglu et al. [64]	0	++ (paraffin and saline) and ± (hydrocolloid)	0	0	0	++ (paraffin and saline) and ± (hydrocolloid)

++: significantly different and in advantage of honey; +: in advantage of honey but not significantly different; ±: no difference between the therapy regimens; –: in disadvantage of honey but not significantly different; ––: significantly different in disadvantage of honey; /: not compared; 0: not reported.

foot ulcers [42]. In this review 19 trials that examined the effects of honey in chronic ulcers were included (Table 3).

Four RCTs, one CT [43] and four CRs [4,44–46] report on the *antibacterial effect* of honey. Only one of the RCTs found a positive effect in favour of honey, however not statistically significant (Tables 4 and 5). The antibacterial action of honey leads to a lower incidence of infection and the elimination of methicillin-resistant Staphylococcus Aureus (MRSA) [34,35].

More evidence could be noticed for the *wound healing stimulating capacity* of honey, for which two out of four RCTs report a statistically significant reduction in wound size (Tables 4 and 5). Two CTs [43,47] and seven CRs [4,44–46,48–50] support the positive effect of honey on wound healing.

The *anti-inflammatory, deodorizing and debridement properties* of honey in ulcers were all supported by one RCT, two CTs [43,47] and multiple CRs; and according to only one RCT honey significantly *reduces wound pain* (Tables 4 and 5). The available evidence for these qualities is therefore weak.

Overall, it can be concluded that the evidence for the antibacterial, anti-inflammatory, deodorizing, debridement and wound pain reducing properties of honey in ulcers is less conclusive. Most evidence had been found for the wound size reducing effect of honey, which was statistically significant in favour of honey in 50% of the trials (Table 5). However, it can be argued if this is enough evidence to make well-substantiated conclusions towards clinical practice.

4.3. *Other wounds*

In this group of wounds with various etiologies 29 studies were included (Table 3).

For the *antibacterial properties* of honey, only one out of five RCTs that investigated this outcome parameter found a statistically significant result in favour of honey (Tables 4 and 5). One CT and seven CRs support this effect of honey [13,26,29,51–55], and two of the CRs report that honey is effective even against MRSA [13,26].

The evidence for the *healing properties* of honey is investigated by twelve RCTs. Four of them report a statistically significant result in favour of honey (Tables 4 and 5). All fourteen case reports support the healing stimulating properties of honey (Table 4).

Six RCTs reported the *anti-inflammatory properties* of honey, and half of them found statistically significant results in favour of honey. The *debriding capacity* of honey is reported in three RCTs, and only in one of them a statistically significant result in favour of honey was found (Tables 4 and 5). Positive results for both of these outcome parameters are respectively supported by one CT and multiple case reports [13,25,26,29,51–58].

Five RCTs report the parameter *wound pain*, but only two of them found a positive result in favour of honey, however not significant (Tables 4 and 5). The *deodorizing properties* of honey are mainly supported by case reports, so the evidence for this property is weak (Tables 4 and 5).

Based on more solid evidence it can be concluded that honey has a stimulating effect on the healing process. Also the anti-inflammatory properties of honey are emphasized. However, for the antibacterial, debridement, and wound pain reducing properties of honey, there is insufficient evidence to make strong conclusions. The superior antibacterial effect of Manuka honey and Medihoney is also not confirmed in this wound category.

5. Discussion

5.1. *Outcomes of the included studies*

Looking at all three described wound categories, it is clear that honey is a dressing with properties that are beneficial to wound healing. However, the evidence for its deodorizing, debridement, anti-inflammatory, and wound pain reducing properties is rather limited.

The evidence for its antibacterial property is strongest in the studies on burns. However, one RCT reported that TE with subsequent grafting leads to a better result [36]. But it is incorrect to compare the effect of topical honey with TE and skin grafting in third degree burns, since honey application is only recommended in first and second superficial degree burns [59,60]. Nevertheless, these findings should be interpreted with caution as five out of seven RCTs were carried out by the same investigator. In six trials a pure, undiluted honey was used, without any specification of its composition. This could be detrimental to the reproducibility and generalization of future research.

For ulcers and other wounds, the evidence for the antibacterial properties of honey is rather moderate to weak, whereby the superior antibacterial effect of Manuka honey and Medihoney is not well substantiated. In general, Manuka honey and Medihoney are recommended for their antibacterial action [4,26–28]. However, in the ulcer wound category for example, 13 trials (3RCTs, 2CTs, 8CRs) used these types of honey (Table 4). Strangely, the antibacterial effect was only reported in nine of them (3RCTs, 1CT, 5CRs), and in only six out of nine (1RCT, 1CT, 4CRs) an antibacterial effect in favour of honey was reported, however without any statistically significance (Table 5). So, based on this limited evidence, the above standing recommendation of these medical honeys cannot be confirmed. Moreover it is striking that the largest and best executed study (Jull et al. [6]) concluded that Manuka honey would not be clinically relevant compared to standard therapy (Table 4).

Another comment is that only few studies in the other wounds category (in this case 2 CRs) investigate honey's elimination capacity towards MRSA [13,26]. In general, studies report the antibacterial properties of honey without further specifications. Nevertheless, given the recent increasing antibiotic resistance it would be very interesting to investigate honey's capacities against several strong and potentially dangerous pathogens, such as MRSA. However, this remark should be interpreted very carefully because this wound category contains wounds of multiple etiologies, by which it is difficult to generalize this conclusion.

In the randomized studies on burns, there is a clear link between the antibacterial effect of honey and the faster wound closure. In the RCTs on other wound types, this link is not always obvious (Table 5). These findings are easy to

explain for burns, as there is no underlying disease present. On the other hand, the underlying factors in chronic wounds can influence the wound healing, even when the wound is clean.

Honey might also be an alternative healing stimulating therapy for chronic ulcers and many other wound types, such as surgical wounds.

In the included RCTs wound type was the main selection criterion. It is also important to separate the study results by wound type and those by type of honey used on the respective wound category, allowing a better comparison between studies and potentially leading to more precise guidelines for future research [61].

When considering the treatment protocol, several considerations must be mentioned. It is remarkable that the type of honey used is sometimes only vaguely described (Table 4). Obviously, the choice of honey is important. In one third of the included studies, even non-medical, non-sterilized honey is being used (Table 4), which implies a potential risk of contamination with impurities [8,18,19]. Standardized usage of the same type of bandage as well as a proper description of the frequency of the dressing changes and mentioning who performed those dressing changes increases the repeatability and generalizability of the study. Deviation from the prescribed protocol undermines the quality and objectivity of the investigation and should be avoided at all times.

In only 12 of the 55 studies (including 6 RCTs), honey is used as a single therapy [25,29,33,36–38,40,41,51,62–64]. In some cases honey was used after certain standard care therapies [63] or in combination with standard wound care [54,65]. Clearly this makes it more difficult to draw conclusions and limits the possibility to repeat and generalize the obtained results. One must know exactly whether the (causal) therapy was equal in both research groups or not, so that the topical treatment (honey or control product) was clearly the only variable in the research made. This allows to conclude that the difference in results between both treatment regimens is only due to the used topical treatment.

In comparing two types of therapy its is also important to perform a proper cost-effectiveness analysis. Although several studies report that honey application reduces the *costs of care* [38,40,41,44,47–50,64,66–73], only one RCT actually calculated the cost-effectiveness of honey and the control therapy by using the Incremental Cost-Effectiveness Ratio (ICER), and it was found to be more profitable for the control therapy [27].

5.2. *Methodology of the included studies*

There is a large variation in sample size between the included studies. To determine the size of the study population, a power analysis was performed in advance in 11 of the 25 RCTs [15,27,34,35,68,69,73–77]. In only 4 of the 11 studies, the required number of participants was recruited [27,68,76,77]. In 3 of 7 other RCTs the necessary number of patients was not achieved due to a difficult recruitment, high costs or expiration of the project duration [15,34,35]. Performing a power analysis on the study population and using strict, however reasonable selection criteria will generate a more homogeneous research group which gives a better chance for representative and valid results [61].

In general, wound related parameters are the most common primary outcomes as wound healing usually is the ultimate goal in wound care [61]. Primary and secondary outcomes should be clearly defined in advance to the benefit of the quality and repeatability of the study [61]. Unfortunately this is not the case for all included studies through which the exact focus of the study is unclear.

Although the same parameters were recorded in the included studies, comparison of the outcomes is rather difficult due to the use of different, and often non-validated measurement methods. Moreover, it is not always clear how and how often the outcome parameters were measured. This contains a risk of measurement bias, which can be corrected by blinding the assessors [61], but in none of the studies such corrections were implemented.

A major limitation in the examination of the use of honey in wound care definitely relates to the lack of blinding due to the obvious smell of honey and the discoloration of the wound bed and surrounding skin [27,34]. Nevertheless, in some randomized investigations both single (8RCTs) [27,28,33,35,39,67,69,75] and double blinding (3RCTs) [68,76,77] were used. Still, one should strive for at least single blinding in wound assessment in the benefit of a qualitative, independent and objective examination of the outcomes [61].

The items issued above are part of the CONSORT statement, developed to enhance the quality of reporting RCTs [78]. The absence of guidelines for other study designs jeopardizes the overall quality assessment. Although there are all sorts of quality scales and scoring systems, it remains a subjective estimation. Designing a standardized scoring scale based on the CONSORT statement could solve this issue.

5.3. *Strengths and weaknesses of this review*

The strength of this review lies in the fact that it provides a global view of the usage of honey in three different wound categories, highlighting the gaps in both results and methodology of the included studies.

Limitations of this review include the inability to carry out a meta-analysis, due to the heterogeneity of the included studies. The literature search could be expanded by also consulting congress papers, expert opinions, books and unpublished papers. However, this systematic review is only based on published literature. Jull et al. [6] also point to the risk of publication bias. Their investigation showed that honey has no added value, which represents a sharp contrast with most other published studies [27].

5.4. *Recommendations for future research*

Evaluating the study materials revealed several gaps in the research for the clinical application of honey in modern wound care. A sufficiently large sample size and treatment period is needed to determine statistical significance, which makes it necessary to perform power analysis and establish larger and well designed randomized trials. When there are differences in baseline characteristics between the study groups, such as wound type, it is important to stratify or to perform corrections for the present confounders.

The applied treatment protocol should be clearly reported and must be respected by each study member. The type of honey used must always be mentioned and must be gamma-sterilized. It is advisable to use honey-impregnated dressings given the ease of use, standard quality and standard composition.

To provide a clear and complete reporting of the results, the CONSORT guidelines for RCTs should be strictly followed. Specific guidelines are equally needed for the other study designs.

To upgrade the evidence on honey in modern wound care, standardized and validated measurement tools are needed, as well as reliable cost-effectiveness analysis, as they will allow a valid comparison with current practice.

Conflict of interest statement

The authors, Lynn Vandamme, Alexander Heyneman, Hendrik Hoeksema, Jozef Verbelen and Stan Monstrey do not have any interests that might be interpreted as influencing the review. This review did not receive any support from industry or private corporations.

REFERENCES

[1] Langemo DK, Hanson D, Anderson J, Thompson P, Hunter S. Use of honey for wound healing. Adv Skin Wound Care 2009;22(March (3)):113–8.
[2] Zumla A, Lulat A. Honey—a remedy rediscovered. J R Soc Med 1989;82(July (7)):384–5.
[3] Bardy J, Slevin NJ, Mais KL, Molassiotis A. A systematic review of honey uses and its potential value within oncology care. J Clin Nurs 2008;17(October (19)):2604–23.
[4] Sare JL. Leg ulcer management with topical medical honey. Br J Community Nurs 2008;13(September (9)):S22, S24, S26.
[5] Dunford C. The use of honey-derived dressings to promote effective wound management. Prof Nurse 2005;20(April (8)):35–8.
[6] Jull AB, Rodgers A, Walker N. Honey as a topical treatment for wounds. Cochrane Database Syst Rev 2008;(4):CD005083. 1–49.
[7] Dany-Mazeau M, Pautard G. L'utilisation du miel dans le processus de cicatrisation. De la ruche à l'hôpital. Krankenpflege Soins infirmiers 1991;84(3):63–9.
[8] Lusby PE, Coombes A, Wilkinson JM. Honey: a potent agent for wound healing? J Wound Ostomy Continence Nurs 2002;29(November (6)):295–300.
[9] Dealey C. Wound management products. In: The care of wounds. A guide for nurses, Third ed., Oxford, UK: Editorial offices: Blackwell Publishing Ltd.; 2005: 83–9.
[10] Dealey C. German Wound Surgeons 1450–1750. EWMA 2005;5(2):48–51.
[11] Bansal V, Medhi B, Pandhi P. Honey–a remedy rediscovered and its therapeutic utility. Kathmandu Univ Med J (KUMJ) 2005;3(July (3)):305–9.
[12] Khan FR, Ul AZ, Rauf N. Honey: nutritional and medicinal value. Int J Clin Pract 2007;61(October (10)):1705–7.
[13] Dunford CE. Treatment of a wound infection in a patient with mantle cell lymphoma. Br J Nurs 2001;10(September (16)):1058, 1060, 1062, 1064–65.
[14] Molan P, Hill C. Quality standards for medical grade honey. In: Cooper R, Molan P, White R, editors. Honey in modern wound management. Aberdeen: Health Comm UK Limited, trading as Wounds UK Limited; 2009. p. 63–79.
[15] Robson V, Dodd S, Thomas S. Standardized antibacterial honey (Medihoney) with standard therapy in wound care: randomized clinical trial. J Adv Nurs 2009;65(March (3)):565–75.
[16] Olaitan PB, Adeleke OE, Ola IO. Honey: a reservoir for microorganisms and an inhibitory agent for microbes. Afr Health Sci 2007;7(September (3)):159–65.
[17] Snowdon JA, Cliver DO. Microorganisms in honey. Int J Food Microbiol 1996;31(August (1–3)):1–26.
[18] Molan PC. Potential of honey in the treatment of wounds and burns. Am J Clin Dermatol 2001;2(1):13–9.
[19] Alcaraz A, Kelly J. Treatment of an infected venous leg ulcer with honey dressings. Br J Nurs 2002;11(July (13)):859–66.
[20] Tan HT, Rahman RA, Gan SH, Halim AS, Hassan SA, Sulaiman SA, et al. The antibacterial properties of Malaysian tualang honey against wound and enteric microorganisms in comparison to manuka honey. BMC Complement Altern Med 2009;9:34.
[21] Henriques A, Jackson S, Cooper R, Burton N. Free radical production and quenching in honeys with wound healing potential. J Antimicrob Chemother 2006;58(October (4)):773–7.
[22] Cooper R. Using honey to inhibit wound pathogens. Nurs Times 2008;104(January (3)):46–9.
[23] Anderson I. Honey dressings in wound care. Nurs Times 2006;102(May (22)):40–2.
[24] Molan P. Honey as a topical antibacterial agent for treatment of infected wounds. World Wide Wounds 2001. Available from: http://www.worldwidewounds.com/2001/november/Molan/honey-as-topical-agent.html [last accessed 15.06.2012] [Internet].
[25] Stephen-Haynes J. Evaluation of a honey-impregnated tulle dressing in primary care. Br J Community Nurs 2004;June (Suppl.):S21–7.
[26] Dunford C, Cooper R, Molan P, White R. The use of honey in wound management. Nurs Stand 2000;15(November (11)):63–8.
[27] Jull A, Walker N, Parag V, Molan P, Rodgers A. Randomized clinical trial of honey-impregnated dressings for venous leg ulcers. Br J Surg 2008;95(February (2)):175–82.
[28] English HK, Pack AR, Molan PC. The effects of manuka honey on plaque and gingivitis: a pilot study. J Int Acad Periodontol 2004;6(April (2)):63–7.
[29] Ahmed AK, Hoekstra MJ, Hage JJ, Karim RB. Honey-medicated dressing: transformation of an ancient remedy into modern therapy. Ann Plast Surg 2003;50(February (2)):143–7.
[30] Simon A, Traynor K, Santos K, Blaser G, Bode U, Molan P. Medical honey for wound care–still the 'latest resort'? Evid Based Complement Alternat Med 2009;6(June (2)):165–73.
[31] Simon A, Sofka K, Wiszniewsky G, Blaser G, Bode U, Fleischhack G. Wound care with antibacterial honey (Medihoney) in pediatric hematology-oncology. Support Care Cancer 2006;14(January (1)):91–7.
[32] White R. The benefits of honey in wound management. Nurs Stand 2005;20(November (10)):57–64.
[33] Moolenaar M, Poorter RL, van der Toorn PP, Lenderink AW, Poortmans P, Egberts AC. The effect of honey compared to conventional treatment on healing of radiotherapy-induced skin toxicity in breast cancer patients. Acta Oncol 2006;45(5):623–4.
[34] Gethin G, Cowman S. Manuka honey vs. hydrogel–a prospective, open label, multicentre, randomised controlled trial to compare desloughing efficacy and healing outcomes in venous ulcers. J Clin Nurs 2009;18(February (3)):466–74.
[35] Gethin G, Cowman S. Bacteriological changes in sloughy venous leg ulcers treated with manuka honey or hydrogel: an RCT. J Wound Care 2008;17(June (6)):241–7.

[36] Subrahmanyam M. Early tangential excision and skin grafting of moderate burns is superior to honey dressing: a prospective randomised trial. Burns 1999;25(December (8)):729–31.
[37] Subrahmanyam M. Honey impregnated gauze versus polyurethane film (OpSite) in the treatment of burns—a prospective randomised study. Br J Plast Surg 1993;46(June (4)):322–3.
[38] Subrahmanyam M. A prospective randomised clinical and histological study of superficial burn wound healing with honey and silver sulfadiazine. Burns 1998;24(March (2)):157–61.
[39] Malik KI, Malik MA, Aslam A. Honey compared with silver sulphadiazine in the treatment of superficial partial-thickness burns. Int Wound J 2010;7(October (5)):413–7.
[40] Subrahmanyam M. Topical application of honey in treatment of burns. Br J Surg 1991;78(April (4)):497–8.
[41] Subrahmanyam M. Honey dressing versus boiled potato peel in the treatment of burns: a prospective randomized study. Burns 1996;22(September (6)):491–3.
[42] Jaul E. Non-healing wounds: the geriatric approach. Arch Gerontol Geriatr 2009;49(September (2)):224–6.
[43] Biglari B, vd Linden PH, Simon A, Aytac S, Gerner HJ, Moghaddam A. Use of Medihoney as a non-surgical therapy for chronic pressure ulcers in patients with spinal cord injury. Spinal Cord 2012;50(February (2)):165–9.
[44] van der Weyden EA. Treatment of a venous leg ulcer with a honey alginate dressing. Br J Community Nurs 2005;Jun (Suppl.):S21. S24, S26–27.
[45] Natarajan S, Williamson D, Grey J, Harding KG, Cooper RA. Healing of an MRSA-colonized, hydroxyurea-induced leg ulcer with honey. J Dermatolog Treat 2001;12(March (1)): 33–6.
[46] Hampton S, Coulborn A, Tadej M, Bree-Aslan C. Using a superabsorbent dressing and antimicrobial for a venous ulcer. Br J Nurs 2011;20(August (15)):S38–40. S43.
[47] Moghazy AM, Shams ME, Adly OA, Abbas AH, El-Badawy MA, Elsakka DM, et al. The clinical and cost effectiveness of bee honey dressing in the treatment of diabetic foot ulcers. Diabetes Res Clin Pract 2010;89(September (3)):276–81.
[48] Hendrickson MA. Utilizing active Leptospermum honey dressings in the treatment of cutaneous small-vessel vasculitis. Ostomy Wound Manage 2010;56(April (4)): 10–2.
[49] van der Weyden EA. The use of honey for the treatment of two patients with pressure ulcers. Br J Community Nurs 2003;8(December (12)):S14–20.
[50] Eddy JJ, Gideonsen MD. Topical honey for diabetic foot ulcers. J Fam Pract 2005;54(June (6)):533–5.
[51] Trudgian J, Trotman S. Ehlers-Danlos syndrome and wound healing: injury in a collagen disorder. Br J Nurs 2011;20(March (6)):S10. S12, S14.
[52] Efem SE. Clinical observations on the wound healing properties of honey. Br J Surg 1988;75(July (7)):679–81.
[53] Cooper RA, Molan PC, Krishnamoorthy L, Harding KG. Manuka honey used to heal a recalcitrant surgical wound. Eur J Clin Microbiol Infect Dis 2001;20(October (10)): 758–9.
[54] Lotfy M, Badra G, Burham W, Alenzi FQ. Combined use of honey, bee propolis and myrrh in healing a deep, infected wound in a patient with diabetes mellitus. Br J Biomed Sci 2006;63(4):171–3.
[55] Rudzka-Nowak A, Luczywek P, Gajos MJ, Piechota M. Application of manuka honey and GENADYNE A4 negative pressure wound therapy system in a 55-year-old woman with extensive phlegmonous and necrotic lesions in the abdominal integuments and lumbar region after traumatic rupture of the colon. Med Sci Monit 2010;16(November (11)):CS138–42.
[56] Robson V, Cooper R. Using leptospermum honey to manage wounds impaired by radiotherapy: a case series. Ostomy Wound Manage 2009;55(January (1)):38–47.
[57] Chernev I, Liguori PA, Senno SL, Peters K, Bree-Aslan C. Combined noncontact, low-frequency ultrasound and medical honey for the treatment of chronic wounds. J Wound Ostomy Continence Nurs 2010;37(4):421–5.
[58] Ganacias-Acuna EF. Active Leptospermum honey and negative pressure wound therapy for nonhealing postsurgical wounds. Ostomy Wound Manage 2010;56(March (3)):10–2.
[59] Subrahmanyam M, Enoch S. Topical application of honey in the treatment of burns. In: Cooper R, Molan P, White R, editors. Honey in modern wound management. Aberdeen: HealthComm UK Limited, trading as Wounds UK Limited; 2009. p. 177–87.
[60] Brusselaers N, Pirayesh A, Hoeksema H, Richters CD, Verbelen J, Beele H, et al. Skin replacement in burn wounds. J Trauma 2010;68(February (2)):490–501.
[61] Gottrup F, Apelqvist J, Price P. Outcomes in controlled and comparative studies on non-healing wounds: recommendations to improve the quality of evidence in wound management. J Wound Care 2010;19(June (6)): 237–68.
[62] Oluwatosin OM, Olabanji JK, Oluwatosin OA, Tijani LA, Onyechi HU. A comparison of topical honey and phenytoin in the treatment of chronic leg ulcers. Afr J Med Med Sci 2000;29(March (1)):31–4.
[63] Schumacher HH. Use of medical honey in patients with chronic venous leg ulcers after split-skin grafting. J Wound Care 2004;13(November (10)):451–2.
[64] Misirlioglu A, Eroglu S, Karacaoglan N, Akan M, Akoz T, Yildirim S. Use of honey as an adjunct in the healing of split-thickness skin graft donor site. Dermatol Surg 2003;29(February (2)):168–72.
[65] Yapucu GU, Eser I. Effectiveness of a honey dressing for healing pressure ulcers. J Wound Ostomy Continence Nurs 2007;34(March (2)):184–90.
[66] Baghel PS, Shukla S, Mathur RK, Randa R. A comparative study to evaluate the effect of honey dressing and silver sulfadiazene dressing on wound healing in burn patients. Indian J Plast Surg 2009;42(July (2)):176–81.
[67] Shukrimi A, Sulaiman AR, Halim AY, Azril A. A comparative study between honey and povidone iodine as dressing solution for Wagner type II diabetic foot ulcers. Med J Malaysia 2008;63(March (1)):44–6.
[68] Ingle R, Levin J, Polinder K. Wound healing with honey—a randomised controlled trial. S Afr Med J 2006;96(September (9)):831–5.
[69] Khanal B, Baliga M, Uppal N. Effect of topical honey on limitation of radiation-induced oral mucositis: an intervention study. Int J Oral Maxillofac Surg 2010;39(December (12)):1181–5.
[70] Al-Waili NS, Saloom KY. Effects of topical honey on post-operative wound infections due to gram positive and gram negative bacteria following caesarean sections and hysterectomies. Eur J Med Res 1999;4(March (3)):126–30.
[71] Okeniyi JA, Olubanjo OO, Ogunlesi TA, Oyelami OA. Comparison of healing of incised abscess wounds with honey and EUSOL dressing. J Altern Complement Med 2005;11(June (3)):511–3.
[72] Mphande AN, Killowe C, Phalira S, Jones HW, Harrison WJ. Effects of honey and sugar dressings on wound healing. J Wound Care 2007;16(July (7)):317–9.
[73] Robson V, Yorke J, Sen RA, Lowe D, Rogers SN. Randomised controlled feasibility trial on the use of medical grade honey following microvascular free tissue transfer to reduce the incidence of wound infection. Br J Oral Maxillofac Surg 2012;50(June (4)):321–7.

[74] Abdulrhman M, El Barbary NS, Ahmed AD, Saeid ER. Honey and a mixture of honey, beeswax, and olive oil-propolis extract in treatment of chemotherapy-induced oral mucositis: a randomized controlled pilot study. Pediatr Hematol Oncol 2012;29(April (3)):285–92.
[75] Lund-Nielsen B, Adamsen L, Kolmos HJ, Rorth M, Tolver A, Gottrup F. The effect of honey-coated bandages compared with silver-coated bandages on treatment of malignant wounds—a randomized study. Wound Repair Regen 2011;19(November (6)):664–70.
[76] McIntosh CD, Thomson CE. Honey dressing versus paraffin tulle gras following toenail surgery. J Wound Care 2006;15(March (3)):133–6.
[77] Chang EH, Alandejani T, Akbari E, Ostry A, Javer A. Double-blinded, randomized, controlled trial of medicated versus nonmedicated merocel sponges for functional endoscopic sinus surgery. J Otolaryngol Head Neck Surg 2011;40(February (Suppl. 1)):S14–9.
[78] Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg 2012;10(1):28–55.
[79] Gethin GT, Cowman S, Conroy RM. The impact of Manuka honey dressings on the surface pH of chronic wounds. Int Wound J 2008;5(June (2)):185–94.
[80] Alese OB, Irabor DO. Pyoderma gangrenosum and ulcerative colitis in the tropics. Rev Soc Bras Med Trop 2008;41(November (6)):664–7.
[81] Hon J. Using honey to heal a chronic wound in a patient with epidermolysis bullosa. Br J Nurs 2005;14(October (19 Suppl.)):S4–12.